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14. ABSTRACT The overall objective of this training program is to provide an opportunity for undergraduate students to spend summer to get exposure to concepts of breast cancer research. We proposed six students to be divided amongst 7-8 faculty members working closely in the area of breast cancer. During the last 3 summers we had introduced the program to the Honors college and GPPA program office. However the project was extended for one more year for the funds left over to train one student. This year we recruited Mr. McCormick for the second summer. He completed a project which will be submitted for publication. He also prepared a short report at the end of the summer and presented a 20 minute departmental seminar. He is interested in continuing to do breast cancer research if he gets an opportunity.					
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Annual Report:

Award No: DAMD 17-03-1-0387

Title: Training Program in Breast Cancer Prevention and Therapy for undergraduate Students

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Dates: May 15, 2007 to August 15, 2008 (Summer Training Only)

Report:

The overall objective of this program is to provide training on the concepts and hands-on laboratory exposure to six undergraduate students who have outstanding credentials and are pursuing their BS degree at the University of Illinois with the intention of joining either medical school or further research career. The program is awarded for training during summer only. This year was an extension for the funds left over from the last year. Therefore only one student was trained this summer.

Task 1: Recruitment of students:

This summer, we had sufficient funds for training only one student. Michael McCormick who also spent summer in our laboratory was recruited this year. We had requests from 4 students, however Mr. McCormick initiated his research project last summer and had expressed desire to complete his assigned project this year. This resulted in selecting Michael McCormick for the summer training this year.

Task 2: assignment of a mentor:

Unlike previous years, we had only one continuing student during this final additional summer period. Dr. Rajendra mehta served as a mentor for Michael McCormick.

Task 3: Conduct research:

During last summer Mr. McCormick had learnt all the necessary procedures needed for chemoprevention research. These included cell culture, MTT and crystal violet assays,

immunofluorescence, flow cytometry, western blot analyses, RT-PCR. Towards the end of the summer Michael was working on a project to determine the reason for inability of vitamin D receptor (VDR) positive steroid receptor negative breast cancer cells. This past summer was very productive and the results generated by Michael will be presented at the Era of hope meeting in Baltimore. The work is summarized in an abstract form below. Dr. Peng in Dr. Mehta's group helped as a supervisor for day to day experiments for Michael McCormick.

Abstract:

Previous studies from our laboratory have shown that estrogen and progesterone receptor positive MCF-7, BT474 and T47D breast cancer cells respond to vitamin D metabolites such as 25-hydroxyvitamin D3, 1,25-dihydroxyvitamin D3 or analogs such as 1 α -hydroxyvitamin D5. The steroid receptor negative MDA-MB231 cells do not exhibit antiproliferative activity in response to vitamin D even though they express vitamin D receptors (VDR) and the expression is upregulated in response to vitamin D. We hypothesized that the histone deacetylation may prevent the VDR from accessing target gene promoters, resulting in the lack of antiproliferative activity. Incubation of MDA-MB231 cells with 15nM of Trichostatin A (TSA) or 25(OH)D3 (250nM) alone had minor effect on cell proliferation as measured by MTT assay. However a combination treatment of TSA and 25(OH)D3 resulted in inhibition of cell growth by >60%. Previous studies in the literature as well as from our laboratory have shown that the antiproliferative effects of vitamin D are accompanied with increased expression of VDR and CYP24, therefore we evaluated the effects of TSA and vitamin D singly and in combination on the mRNA expression of VDR, CYP24 and CYP27B1 in these cells using quantitative RT-PCR analysis. Results showed that TSA alone inhibited the expression of CYP24, 25(OH)D3 alone enhanced CYP24 expression by 115 fold, whereas the combination of TSA and 25(OH)D3 enhanced expression of CYP24 by 137 fold. These results indicate that inhibition of histone deacetylation by TSA in these cells make them responsive to 25(OH)D3. We expanded these studies to determine if any of the known chemopreventive agents derived from natural products can serve as histone deacetylation inhibitors in these cells. We evaluated effects of epigallocatechin gallate, sulforaphan, diallyl disulfide and butyric acid. However none of these agents were comparable for the histone deacetylation inhibiting properties of TSA. These results indicate that inhibition of histone deacetylation for VDR positive vitamin D non-responsive cells may provide useful strategy for vitamin D responsiveness.

Task 4: Completion of training period:

The work completed by the student was presented in the form of a seminar. The students in the previous years were asked to provide verbal evaluation of the program. Mr. McCormick also indicated that the program was very useful in getting him to decide that he would like to pursue research in the area of breast cancer if the opportunity arises.

Accomplishments:

- Michael McCormick was the only undergraduate recruited as a trainee during the past summer.
- He spent 2 summers as a part of this program in the laboratory and generated valuable results.
- The results generated will be submitted for publication. For now, the abstracts are being considered for presentation at Era of Hope and AACR meeting.

Update and accomplishments of Students from the past years' training

- Neil Patel and Daniel Czyz were invited to present their work (started as summer trainee and continued) at the ERA of Hope meeting in Philadelphia
- Daniel Czyz joined PhD program at Northwestern University, Chicago in Biochemistry
- Pavan Jhaveri joined Baylor Medical School for MD
- Juliana Choi was a GPPA MD student, now started working as a MD, PhD student in the department.
- Sonali Patel was a student at IIT, completed BS and is now a MD student at Rush Medical School in Chicago.
- Michael McCormick started last year and continued this summer

Reportable Outcomes:

The students learnt and understood procedures in the laboratories. Since they were all assigned projects, if the results are published in a scientific journal with new additional data, then the student will get the credit.

Conclusions:

- The training program is an excellent way to introduce students who are curious to learn about research methods in breast cancer research.
- Our experience suggests that the students who are motivated perform to the best of their ability and feel accomplished that they have learnt new procedures and have clearly indicated that they may want to do research in breast cancer.
- Two of our past students presented their work at the DOD meeting of Era of Hope conference and got an outstanding exposure. One joined a PhD program at Northwestern University. One abstract from the current student is submitted to era of Hope meeting to be held in Baltimore in 2008.

